MECHANISMS AND FUNCTIONS OF SEROTONIN NEURONAL SYSTEMS: OPPORTUNITIES FOR NEUROPEPTIDE INTERACTIONS. R. W. Fuller. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46285.

Serotonin neurons project from the raphe nuclei in the brain stem to almost all areas of the brain and the spinal cord (Jacobs and Azmitia, Physiol. Rev. 72, 165-229, 1992). Consequently, serotonin neurons can modulate many different physiological functions controlled by the brain. Serotonin nerve terminals synthesize, store and release serotonin, and specific transporters on the terminals remove serotonin from the synaptic cleft to limit its actions on target receptors. Some serotonin nerve terminals in the brain do not form tight synaptic junctions with target neurons but instead may influence a field of neurons by "drip-irrigation" (Tork, Ann. N. Y. Acad. Sci. 600, 9, 1990). Drugs that alter the function of serotonin neurons with high selectivity (including uptake inhibitors and specific receptor agonists or antagonists) have facilitated study of their physiological roles and have contributed importantly to the treatment of psychiatric and other diseases. One major development in serotonin pharmacology during recent years has been the elucidation of multiple serotonin receptor subtypes. At least fourteen have been cloned: $5HT_{1A}$, $5HT_{1B}$ (or $5HT_{1D\beta}$), $5HT_{1D}$ (or $5HT_{1D\alpha}$), $5HT_{1E}$, $5HT_{1F}$, $5HT_{2A}$, $5HT_{2B}$, $5HT_{2C}$, $5HT_3$, $5HT_4$, $5HT_{5A}$, $5HT_{5B}$, $5HT_6$ and $5HT_7$, and others are likely to be discovered (Hoyer *et. al.*, Pharmacol. Rev. 46, 157, 1994). The search is underway for agents that interact selectively as agonists or antagonists with each of these receptors. Serotonin co-exists in some neurons with one or more neuropeptides, including somatostatin, enkephalin, substance P, thyrotropin-releasing hormone, galanin and calcitonin gene-related peptide. The peptide cotransmitters might influence serotonin's actions on certain of these receptor subtypes or otherwise modulate serotonin function. Also, serotonergic input to peptidergic neurons might affect the synthesis, release or functions of specific neuropeptides, and peptidergic input may alter the synthesis, release or functions of serotonin. Particularly because serotonin influences appetite, pain, hormone secretion and other things that neuropeptides also influence, the number of known interactions of these sorts is likely to grow.

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